

A9. NON – INVASIVE REALTIME *IN VIVO* IMAGING OF OESTROGEN RECEPTOR ACTIVATION AND BREAST CANCER METASTASIS¹

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Through intracellular receptors, oestrogens control growth, differentiation and the function of not only reproductive tissues, but also other systems. Oestrogen receptors are ligand-dependent transcription factors whose activity is modulated either by oestrogens, or by alternative intracellular signalling pathways downstream of growth factors and neurotransmitters. To determine the dynamics of oestrogen receptor activity and the dependence of the oestrogen receptor on 17-oestradiol *in vivo*, we generated a transgenic mouse that

expresses a luciferase reporter gene under the control of activated oestrogen receptors. As expected, luciferase activity, monitored with a cooled charged-coupled device camera, paralleled circulating oestrogen levels in reproductive tissues and in liver, indicating that the peak transcriptional activity of the oestrogen receptor occurred at proestrus. In contrast, in tissues such as bone and brain, the peak activity of oestrogen receptors was observed at diestrus. These tissue-specific responses are masked when mice undergo conventional hormone treatment. We also demonstrated that oestrogen receptors are active in immature mice before gonadal production of sex hormones, as well as in ovariectomised adult mice. These findings emphasise the importance of hormone-independent activation of the oestrogen receptor, and have implications for the therapeutic use of oestrogens, such as hormone replacement therapy.

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